

September 23, 2002

Ton van Dongen
Corporate Manager
PURAC America Inc.
Arkelsedijk 46
P.O. Box21
4200 AA Gorinchem
The Netherlands

Dear Mr. Dongen:

The Office of Pollution and Toxics is transmitting EPA's comments on the robust summaries and test plan for Lactic Acid, posted on the ChemRTK HPV Challenge Program Web site on February 20, 2002. I commend PURAC America Inc. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that PURAC America Inc. advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
A. Abramson
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission: Lactic Acid

SUMMARY OF EPA COMMENTS

The sponsor, PURAC America Inc., submitted a test plan and robust summaries to EPA for lactic acid (CAS No. 50-21-5) on January 4, 2002. EPA posted the submission on the Chemical RTK HPV Challenge Web site on February 20, 2002.

EPA has reviewed the submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. The submitter needs to supply the results of fugacity and photodegradation calculations in robust summary format. All other SIDS-level endpoints have been addressed for the purposes of the HPV Challenge Program.
2. Health Effects. Adequate data are available for acute, repeated-dose, and genetic (chromosomal aberrations) toxicity for the purposes of the HPV Challenge Program. Although data for developmental toxicity and gene mutations are inadequate and no data are available for reproductive toxicity, no additional testing is needed for these endpoints because the chemical is a product of mammalian metabolism.
3. Ecological Effects. All SIDS-level endpoints have been met for the purpose of the HPV Challenge Program. The submitter needs to provide missing data elements in the robust summaries.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE LACTIC ACID CHALLENGE SUBMISSION

Substance Identity

The submitter states that most lactic acid is manufactured as the natural (+)-isomer and reports the information on that basis. EPA agrees with this approach. [While these data do not automatically apply to the unnatural (-)-isomer, the unnatural isomer would probably not act significantly differently in this case].

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

All appropriate SIDS-level endpoints have been addressed for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Adequate data are available for biodegradation and stability in water. The submitter needs to supply fugacity and photodegradation calculations.

Photodegradation. Although direct photolysis is not expected because lactic acid does not absorb UV light above 290 nm, photodegradation estimates through reaction with hydroxyl radicals need to be provided. The Atmospheric Oxidation Potential (AOPWIN v.1.90) program in EPIWIN v.3.10 can be used to address this endpoint.

Fugacity. The submitter supplied no data for this endpoint in the robust summaries or the test plan, arguing that lactic acid's high water solubility and its biodegradability make the determination

unnecessary. However, this rudimentary intuitive analysis provides no useful information as to the relative importance of partitioning to soil or sediment. EPA recommends that the submitter provide transport/distribution model results, preferably using a Level III fugacity model, in robust summary format. This should include the assumptions and data inputs, using measured data where available.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate data are available for acute, repeated-dose, and genetic toxicity (chromosomal aberrations) for the purposes of the HPV Challenge Program. The information presented in the robust summaries for gene mutations and developmental toxicity is insufficient to judge the adequacy of the data, and no data are available for reproductive toxicity. No further testing was proposed by the submitter, who states that even where there are insufficient data for a given endpoint, testing is unnecessary because lactic acid is a normal human metabolite of low toxicity. EPA agrees that no testing is needed for these endpoints based on lactic acid's role in normal human metabolism.

Genetic Toxicity (in vitro). Gene Mutations. The adequacy of the data cannot be determined because the robust summary was poorly documented.

Reproductive/Developmental Toxicity. Data submitted for developmental toxicity are inadequate because the study evaluated the influence of lactate on the potential developmental effects of aluminum-containing compounds. No data are available for reproductive toxicity, and no testing is proposed. Because the substance is a normal component of intermediary human metabolism, EPA agrees that no additional SIDS-level testing is necessary for these endpoints.

Ecological Effects (fish, invertebrate and algae).

EPA would have preferred that the test substance be the neutralized form (to pH 7) for all aquatic testing, but given that the most toxic form (non-neutralized) of the substance was tested and all effects with the exception of algae occurred at >100 mg/L, EPA in this case accepts the data as adequate for the purpose for the HPV Challenge Program. The submitter needs to indicate, where applicable, that these tests were conducted using the non-neutralized form of the test substance.

Specific Comments on Robust Summaries

Physicochemical Properties

Melting Point. For completeness, the submitter should include the melting point for the anhydrous form of the racemic mixture.

Health Effects.

Acute Toxicity. The omitted information includes the purity of the test material, gavage vehicle, period of post-treatment observation, incidence of mortality, systemic toxicity in target organs by dose and sex, and method of LD₅₀ calculation.

Repeated-Dose Toxicity. Missing information includes method details, group sizes, frequency of data collection (for clinical signs, body weight, and food and water intake), endpoints examined (hematology, clinical chemistry, gross pathology and histopathology), specific organs that were weighed and examined histologically, and statistical methods.

Genetic Toxicity (in vitro). Information missing for bacterial mutations and chromosomal aberrations included concentrations tested, the positive and negative controls, the source of the metabolic activation system, the number of cells examined, the duration of exposure, and the criteria for positive and negative results.

Ecological Effects.

Fish. The submitter needs to provide missing data elements including water temperature, water hardness, alkalinity, dissolved oxygen, and pH levels.

Invertebrates. The submitter needs to provide missing data elements including water temperature, water hardness, dissolved oxygen, and pH levels.

Aquatic plants. The submitter needs to provide missing data elements including pH, temperature, lighting conditions, composition of growth medium, water hardness, dissolved oxygen, and state whether the chemical was neutralized at pH 7.0.

Follow-up Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.